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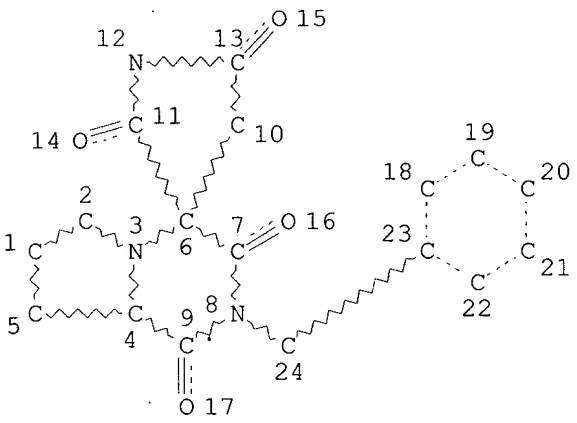
L1 STR



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DEFAULT MLEVEL IS ATOM
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L3 31 SEA FILE=REGISTRY SSS FUL L1
L4 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

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L4 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:866705 HCAPLUS
DOCUMENT NUMBER: 134:157023
TITLE: Influence of temperature on enantioseparation employing an amylose-derivative stationary phase
AUTHOR(S): Kazusaki, Masato; Kawabata, Hirofumi; Matsukura, Hayashi
CORPORATE SOURCE: Department of Chemical Analysis, Pharmaceutical Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Fukushima-ku, Osaka, 553-0001, Japan
SOURCE: J. Liq. Chromatogr. Relat. Technol. (2000), 23(19), 2937-2946
CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In reversed-phase mode, chromatog. retention was studied thermodynamically for an enantiomeric pair on an amylose-deriv. bonded phase. Enthalpies and entropies of solute transfer (mobile to stationary phase) are calcd. from retention data by evaluation of van't Hoff plots. Conformational change of the stationary phase is obsd. at .apprx.20.degree.C. The enantioselectivity is exclusively driven by enthalpy .gtorsim.20.degree.C, whereas .ltorsim.20.degree.C enantiosepn. was achieved by the combination of enthalpy and entropy. The inclusion process of the enantiomer, retained stronger on the stationary phase, plays an important role for chiral recognition on the amylose-derived stationary phase.
IT **147193-59-7 147254-64-6 147254-65-7**
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); PRP (Properties); ANST (Analytical study); PROC (Process)
(solute; influence of temp. on enantiosepn. employing an amylose-deriv. stationary phase)
REFERENCE COUNT: 9
REFERENCE(S): (1) Feibush, B; J Am Chem Soc 1986, V108, P3310 HCAPLUS
(2) Francotte, E; J Chromatogr 1985, V347, P25 HCAPLUS
(3) Isaksson, R; J Chromatogr 1990, V498, P257 HCAPLUS
(4) Lipkowitz, K; J Am Chem Soc 1997, V119, P600 HCAPLUS
(5) Negoro, T; J Med Chem 1998, V41, P4118 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:775488 HCAPLUS
DOCUMENT NUMBER: 134:9445
TITLE: Comparative study of amylose and cellulose derivatized chiral stationary phases in the reversed-phase mode
AUTHOR(S): Kazusaki, Masato; Kawabata, Hirofumi; Matsukura, Hayashi
CORPORATE SOURCE: Department of Chemical Analysis Pharmaceutical Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Osaka, 553-0001, Japan
SOURCE: J. Liq. Chromatogr. Relat. Technol. (2000), 23(18), 2819-2828
CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A direct, isocratic, and simple reversed-phase HPLC method was described for the sepn. of enantiomers, the newly synthesized potential drug

substance and corresponding optical impurity, employing polysaccharide-based chiral stationary phases (Chiralpak AD-RH and Chiralcel OD-RH). A baseline sepn. was attained with both columns. These two chiral stationary phases exhibit opposite chiral discrimination patterns concerning the elution order of enantiomers. Chiralpak AD-RH is more suitable for resolving the enantiomers. Low level quantification (0.05%) of the minor enantiomer is achieved. The anal. procedure was successfully applied to the detection of the optical impurity in a potential drug substance. The minor enantiomer was not detd. quant. because of a trace level of it in the potential drug substances.

IT **147193-59-7 147254-64-6 147254-65-7**
RL: ANT (Analyte); ANST (Analytical study)
(comparative study of amylose and cellulose derivatized chiral stationary phases in reversed-phase mode)

REFERENCE COUNT: 9
REFERENCE(S):
(2) Caldwell, J; J Chromatogr A 1995, V694, P39 HCAPLUS
(3) Caldwell, J; J Chromatogr A 1996, V719, P3 HCAPLUS
(4) Ishikawa, A; J Liq Chromatogr 1993, V16, P859 HCAPLUS
(5) Negoro, T; J Med Chem 1998, V41, P4118 HCAPLUS
(6) Okamoto, Y; J Chromatogr 1987, V389, P95 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:553418 HCAPLUS
DOCUMENT NUMBER: 133:144931
TITLE: Use of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors for the manufacture of a medicament for the treatment of diabetic neuropathy
INVENTOR(S): Cameron, Norman Eugene; Cotter, Mary Anne
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; University Court of the University of Aberdeen
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000045818	A1	20000810	WO 2000-GB280	20000201

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-2591 A 19990206
GB 1999-2594 A 19990206

AB The invention relates to a new use of a statin drug in the improvement of diabetic neuropathy, specifically in improving nerve conduction velocity and nerve blood flow in patients suffering diabetes, in particular to pharmaceutical combinations of the statin drug and other agents known to improve diabetic neuropathy such as an aldose reductase inhibitor, an angiotensin converting enzyme inhibitor, or an angiotensin II antagonist, which combinations are useful in the prevention and treatment of the complications of diabetes.

IT **147254-64-6**, AS-3201
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HMG-CoA reductase inhibitors for treatment of diabetic neuropathy, and

combinations with other agents)
REFERENCE COUNT: 3
REFERENCE(S): (1) E R Squibb & Sons Inc; EP 0482498 A 1992 HCAPLUS
(2) E R Squibb & Sons Inc; US 5130333 A 1992 HCAPLUS
(3) Shionogi Seiyaku Kabushiki Kaisha; EP 0521471 A 1993 HCAPLUS

L4 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:283116 HCAPLUS
DOCUMENT NUMBER: 133:171661
TITLE: AS-3201: Aldose reductase inhibitor
AUTHOR(S): Ono, Yoshiyuki; Negoro, Toshiyuki; Komiya, Masanobu
CORPORATE SOURCE: Clinical Development Division, Dainippon Pharmaceutical Co., Ltd., Suita, 564-0053, Japan
SOURCE: Drugs Future (2000), 25(2), 131-136
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 19 refs. on the synthesis and pharmacol. action of the title agent. At present, AS-3201 is under phase II clin. evaluation for diabetic peripheral neuropathy.
IT **147254-64-6P**, AS-3201
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(AS-3201: aAldose reductase inhibitor)
REFERENCE COUNT: 19
REFERENCE(S): (1) Brownlee, M; Diabetes 1994, V43, P836 HCAPLUS
(2) Cameron, N; Br J Pharmacol 1992, V107, P939 HCAPLUS
(7) Greene, D; J Clin Invest 1983, V72, P1058 HCAPLUS
(12) Negoro, T; J Med Chem 1998, V41, P4118 HCAPLUS
(16) Stevens, M; J Clin Invest 1994, V94, P853 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:282098 HCAPLUS
DOCUMENT NUMBER: 130:316650
TITLE: Rapidly soluble drug composition
INVENTOR(S): Ohashi, Mamoru; Ogasawara, Kazuyoshi; Shirai, Yoshimi; Fujioka, Hiroshi
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920277	A1	19990429	WO 1998-JP4658	19981015
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9894619	A1	19990510	AU 1998-94619	19981015
EP 1033132	A1	20000906	EP 1998-947883	19981015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LV, FI, RO				
BR 9814090	A	20001003	BR 1998-14090	19981015

NO 2000002049 A 20000619 NO 2000-2049 20000418
PRIORITY APPLN. INFO.: JP 1997-306635 A 19971020
WO 1998-JP4658 W 19981015

AB The invention relates to a rapidly sol. drug compn. contg. pulverized (R)-2-(4 -bromo-2-fluorobenzyl)-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4 -spiro-3'-pyrrolidine-1,2',3,5'-tetraone (AS-3201). It is improve d in dissoln. and has a good bioavailability.

IT **147254-64-6**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(rapidly sol. drug compn.)

REFERENCE COUNT: 5
REFERENCE(S):
(1) Anon; Design and Evaluation of Peroral Pharmaceutical Preparations 1995, P81
(2) Anon; Practical Drug Additives" 1974, P258
(3) Dainippon Pharmaceutical Co Ltd; EP 520320 A2 HCAPLUS
(4) Dainippon Pharmaceutical Co Ltd; US 5258382 A HCAPLUS
(5) Dainippon Pharmaceutical Co Ltd; JP 05186472 A 1996 HCAPLUS

L4 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:282097 HCAPLUS
DOCUMENT NUMBER: 130:316649
TITLE: Stable drug composition
INVENTOR(S): Ohashi, Mamoru; Ogasawara, Kazuyoshi; Shirai, Yoshimi; Fujioka, Hiroshi
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920276	A1	19990429	WO 1998-JP4657	19981015
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9894618	A1	19990510	AU 1998-94618	19981015
EP 1038525	A1	20000927	EP 1998-947882	19981015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: JP 1997-306634 A 19971020
WO 1998-JP4657 W 19981015

AB The invention relates to a stable drug compn. of (R)-2-(4-bromo-2-fluorobenzyl)-1,2,3 ,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine-1,2',3 ,5'-tetraone (referred to as AS-3201), which contains a stabilizer comprising at least one acidic substance having an acidity higher than that of AS-3201, such as ascorbic acid, citric acid, tartaric acid, lactic acid, maleic acid, malic acid or phosphoric acid.

IT **147254-64-6**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stable drug compn.)

REFERENCE COUNT: 4
REFERENCE(S):
(1) Anon; Practical Drug Additives 1974, P215
(2) Dainippon Pharmaceutical Co Ltd; EP 520320 A2

HCAPLUS
(3) Dainippon Pharmaceutical Co Ltd; US 5258382 A HCAPLUS
(4) Dainippon Pharmaceutical Co Ltd; JP 05186472 A 1996 HCAPLUS

L4 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:595160 HCAPLUS
DOCUMENT NUMBER: 129:302570
TITLE: Novel, Highly Potent Aldose Reductase Inhibitors: (R)-(-)-2-(4-Bromo-2-fluorobenzyl)-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine- 4-spiro-3'-pyrrolidine-1,2',3,5'-tetrone (AS-3201) and Its Congeners
AUTHOR(S): Negoro, Toshiyuki; Murata, Makoto; Ueda, Shozo; Fujitani, Buichi; Ono, Yoshiyuki; Kuromiya, Akemi; Komiya, Masanobu; Suzuki, Kenji; Matsumoto, Jun-ichi
CORPORATE SOURCE: Department of Chemistry I, Discovery Research Laboratories I Dainippon Pharmaceutical Company Ltd., Suita/Osaka, 564-0053, Japan
SOURCE: J. Med. Chem. (1998), 41(21), 4118-4129
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of novel tetrahydropyrrolo[1,2-a]pyrazine derivs. were synthesized and evaluated as aldose reductase inhibitors on the basis of their abilities to inhibit porcine lens aldose reductase in vitro and to inhibit sorbitol accumulation in the sciatic nerve of streptozotocin-induced diabetic rats in vivo. Of these compds., spirosuccinimide-fused tetrahydropyrrolo[1,2-a]pyrazine-1,3-dione derivs. showed significantly potent aldose reductase inhibitory activity. In the in vivo activity of these derivs., 2-(4-bromo-2-fluorobenzyl)-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine-1,2',3,5'-tetrone (I) (SX-3030) showed the best oral activity. The enantiomers of I were synthesized, and the biol. activities were evaluated. It was found that aldose reductase inhibitory activity resides in the (-)-I (AS-3201), which was 10 times more potent in inhibition of the aldose reductase (IC50 = 1.5 .times. 10-8 M) and 500 times more potent in the in vivo activity (ED50 = 0.18 mg/kg/day for 5 days) than the corresponding (+)-I (SX-3202). From these results, AS-3201 was selected as the candidate for clin. development. The abs. configuration of AS-3201 was also established to be (R)-form by single-crystal X-ray anal. In this article we report the prepn. and structure-activity relationship of tetrahydropyrrolopyrazine derivs. including a novel aldose reductase inhibitor, AS-3201.

IT **147254-64-6P 147254-65-7P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and aldose reductase-inhibiting activity of (bromofluorobenzyl]spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]tetrone AS-3201 and its congeners)

IT **147193-59-7P 147193-74-6P 147193-75-7P 147193-76-8P 147193-79-1P 147193-81-5P 156141-93-4P 156141-94-5P 156142-16-4P 156142-17-5P 156142-18-6P 156142-19-7P 156142-20-0P 156142-21-1P 156142-22-2P 156142-23-3P 156142-24-4P 156142-25-5P 156142-26-6P 156142-27-7P 156142-28-8P 156142-30-2P 156142-32-4P 214418-34-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and aldose reductase-inhibiting activity of (bromofluorobenzyl]spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]tetrone AS-3201 and its congeners)

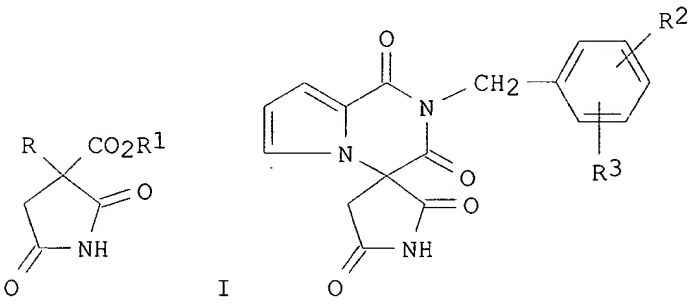
IT **147193-82-6P 156142-31-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and aldose reductase-inhibiting activity of
(bromofluorobenzyl]spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-
a]pyrazine]tetrone AS-3201 and its congeners)

L4 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:207565 HCAPLUS
DOCUMENT NUMBER: 122:9860
TITLE: Preparation of 2-amino-2-carboxysuccinimide derivatives as intermediate for aldose reductase inhibitors
INVENTOR(S): Negoro, Toshuki; Murata, Makoto; Ueda, Shozo; Fujitani, Buichi; Ono, Yoshuki
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06192222	A2	19940712	JP 1992-358941	19921225

OTHER SOURCE(S): MARPAT 122:9860
GI



AB The title compds. (I; R1 = tert-butoxylcarbonylamino, pyrrol-yl, NH2 protected by a group which can be cleaved by hydrogenolysis; R1 = CO2H-protective group), useful as intermediates for noble spiro[tetrahydropyrrolo[1,2-a]pyrazine-4,3'-pyrrolidine] derivs. (II; R2 = H, halo; R3 = halo) having potent inhibitory activity against aldose reductase, are prepd. Thus, di-Et 2-benzyloxycarbonylaminomalonate was refluxed with tert-Bu bromoacetate and K2CO3 in acetone for 7 h to give 92.0% di-Et 2-benzyloxycarbonylamino-2-tert-butoxylcarbonylmethylmalonate which was treated with CF3CO2H in CHCl3 at 50.degree. for 2 h to give 90.2% 2-benzyloxycarbonylamino-2-carboxymethylmalonate followed by chlorination with SOCl2 in CHCl3 contg. DMF and amidation with aq. NH3 in CHCl3 to give 97.7% 2-benzyloxycarbonylamino-2-carbamoylmethylmalonate. This was stirred with EtONa in EtOH under ice-cooling for 1 h to give title compd. I (R = PhCH2O2CNH, R1 = Et) (III) which was resolved by cinchonidine by preferential crystn. of (-)-III.cinchonidine salt from EtOH to give, after acidification with 5% aq. HCl in EtOAc, (-)-III. The latter enantiomer was converted into (-)-II (R2 = 2-F, R3 = 4-Br) which in vitro showed IC50 of 0.039 .mu.M against aldose reductase vs. 0.050 .mu.M for the racemate.

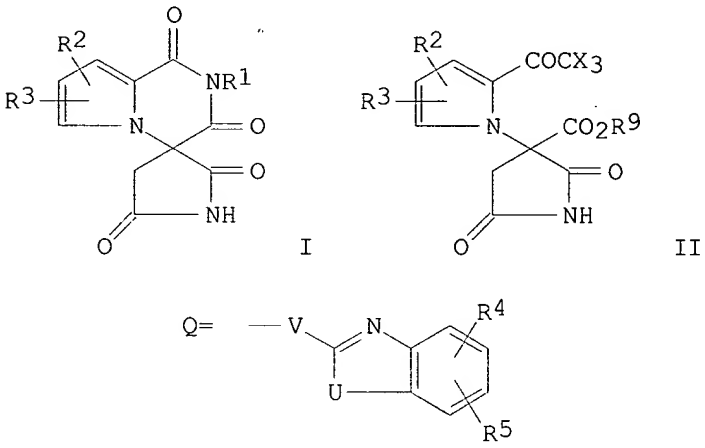
IT **147193-59-7P 147254-64-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aldose reductase inhibitor and 2-amino-2-carboxysuccinimide

deriv. intermediate)

L4 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:483373 HCAPLUS
DOCUMENT NUMBER: 121:83373
TITLE: Preparation of aldose reductase-inhibiting tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidines and their intermediates
INVENTOR(S): Negoro, Toshuki; Murata, Makoto; Ueda, Shozo; Fujitani, Buichi; Ono, Yoshuki
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05345784	A2	19931227	JP 1992-280653	19920925
JP 3022693	B2	20000321		

OTHER SOURCE(S): MARPAT 121:83373
GI



AB The title compds. I [R1 = H, lower alkyl, (substituted) aralkyl, (substituted) aryl, Q; R2, R3 = H, halo, lower alkyl, lower alkoxy, acyl, nitro, amino, lower (di)alkylamino, (substituted) aryl; if R2 or R3 = H, other = H, halo, lower alkyl, then R1 .noteq. (halo-, CF3-, lower alkyl-, lower alkoxy-, nitro-substituted) benzyl; R4, R5 = H, halo, CF3, lower alkyl, lower alkoxy, acyl, nitro, amino, lower (di)alkylamino; U = O, S, NR6; R6 = H, lower alkyl; V = lower alkylene], their salts, and their intermediates II (R2, R3 = same as I; R9 = protective group, X = halo) are prepd. II (R2 = 4-Ac, R3 = H, R9 = Et, X = Cl) (prepn. given) was treated with 4-bromo-2-fluorobenzylamine.HCl and NEt3 in DMF at room temp. for 20 h to give 12.3% I (R1 = 4-bromo-2-fluorobenzyl, R2 = 7-Ac, R3 = H). I (R1 = 4-bromo-2-fluorobenzyl, R2 = 6-Br, R3 = 7-Br) inhibited aldose reductase in vitro with IC50 of 0.052 .mu.M.

IT **156142-15-3P**, 2-(4-Bromo-2-fluorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and bromination of)

IT **156142-16-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)

IT **156142-17-5P**, 2-(2-Chlorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone **156142-18-6P** **156142-19-7P** **156142-20-0P** **156142-21-1P** **156142-22-2P** **156142-23-3P** **156142-24-4P** **156142-25-5P** **156142-26-6P** **156142-27-7P** **156142-28-8P** **156142-29-9P** **156142-30-2P**, 2-(4-Bromo-2-fluorobenzyl)-7-chloro-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone **156142-31-3P**, 7-Bromo-2-(4-bromo-2-fluorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone **156142-32-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

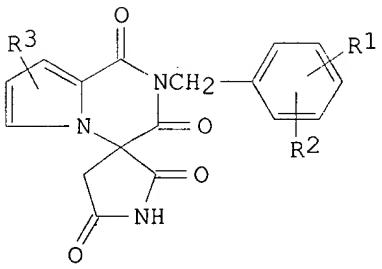
IT **156141-85-4P**, 7-Acetyl-2-(4-bromo-2-fluorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone **156141-93-4P**, 6,7-Dibromo-2-(4-bromo-2-fluorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone **156141-94-5P**, 2-(4-Aminobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as aldose reductase inhibitor)

L4 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:234091 HCAPLUS
DOCUMENT NUMBER: 118:234091
TITLE: Preparation of tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine derivatives as aldose reductase inhibitors
INVENTOR(S): Negoro, Toshiyuki; Murata, Makoto; Ueda, Shozo; Fujitani, Buichi; Ono, Yoshiyuki
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 520320	A2	19921230	EP 1992-110270	19920617
EP 520320	A3	19930324		
EP 520320	B1	19970910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
CA 2071273	AA	19921227	CA 1992-2071273	19920615
ZA 9204425	A	19930331	ZA 1992-4425	19920617
AT 157980	E	19970915	AT 1992-110270	19920617
ES 2108717	T3	19980101	ES 1992-110270	19920617
FI 98066	B	19961231	FI 1992-2848	19920618
FI 98066	C	19970410		
US 5258382	A	19931102	US 1992-901029	19920619
AU 9218483	A1	19930114	AU 1992-18483	19920624
AU 648901	B2	19940505		
HU 63424	A2	19930830	HU 1992-2105	19920624
HU 218214	B	20000628		
NO 9202512	A	19921228	NO 1992-2512	19920625
JP 05186472	A2	19930727	JP 1992-193074	19920625
JP 2516147	B2	19960710		
CN 1068825	A	19930210	CN 1992-108832	19920626
CN 1034176	B	19970305		

PRIORITY APPLN. INFO.: JP 1991-183185 A 19910626
OTHER SOURCE(S): MARPAT 118:234091

GI



I

AB Title compds. (R1, R2 = H, halo, F3C, C1-6 alkyl, C1-6 alkoxy, O2N; R3 = H, halo, C1-6 alkyl) or a salt thereof, are prepd. 2-(Ethoxycarbonyl)-2-(2-trichloroacetylpyrrol-1-yl)succinimide, 4,2-BrFC6H3CH2NH2.HCl and Et3N in anhyd. DMF were stirred for 20 h at 25.degree. to give I (R1 = 2-F, R2 = 4-Br, R3 = H). A similar prepd. title compd. I (R1 = 3-Cl, R2 = R3 = H) inhibited aldose reductase with IC50 0.031 .mu.M. Pharmaceutical formulations comprising I were given.

IT **147193-59-7P 147193-60-0P 147193-61-1P**
147193-62-2P 147193-63-3P 147193-64-4P
147193-65-5P 147193-66-6P 147193-67-7P
147193-68-8P 147193-69-9P 147193-70-2P
147193-71-3P 147193-72-4P 147193-73-5P
147193-74-6P 147193-75-7P 147193-76-8P
147193-77-9P 147193-78-0P 147193-79-1P
147193-80-4P 147193-81-5P 147193-82-6P
147254-64-6P 147254-65-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as aldose reductase inhibitor)

=>

=>

=> fil caold

FILE 'CAOLD' ENTERED AT 18:41:04 ON 12 JUL 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=>

=>

=> s l3

L7 0 L3

=>

=>

=> fil reg

FILE 'REGISTRY' ENTERED AT 18:41:32 ON 12 JUL 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 11 JUL 2001 HIGHEST RN 345580-38-3
DICTIONARY FILE UPDATES: 11 JUL 2001 HIGHEST RN 345580-38-3

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=>

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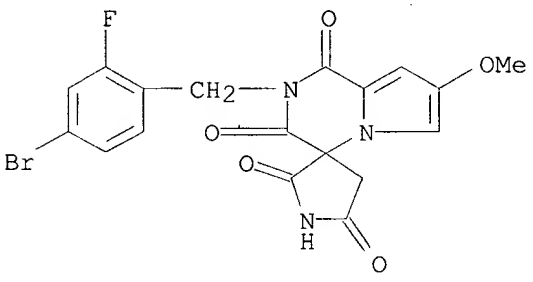
=> d ide can l3 tot

L3 ANSWER 1 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 214418-34-5 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]-7'-methoxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H13 Br F N3 O5
SR CA
LC STN Files: CA, CAPLUS

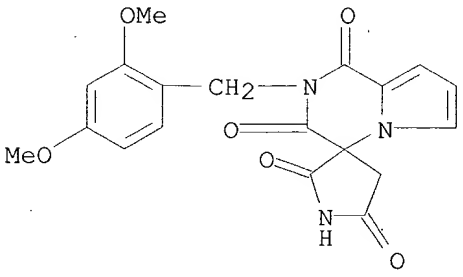


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

L3 ANSWER 2 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-32-4 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(2,4-dimethoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

FS 3D CONCORD
DR 147193-72-4
MF C19 H17 N3 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

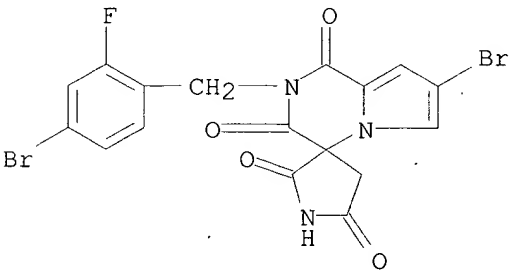


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 3 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-31-3 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 7'-bromo-2'-[(4-bromo-2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 7-Bromo-2-(4-bromo-2-fluorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone
FS 3D CONCORD
DR 147193-78-0
MF C17 H10 Br2 F N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



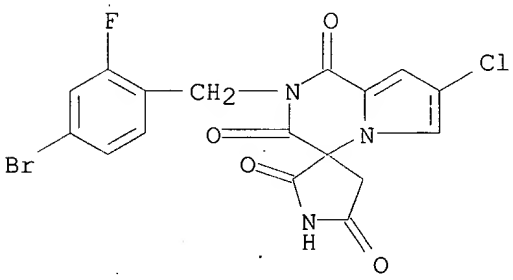
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 4 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-30-2 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]-7'-chloro- (9CI) (CA INDEX NAME)
OTHER NAMES:

CN 2-(4-Bromo-2-fluorobenzyl)-7-chloro-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone
FS 3D CONCORD
DR 147193-77-9
MF C17 H10 Br Cl F N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

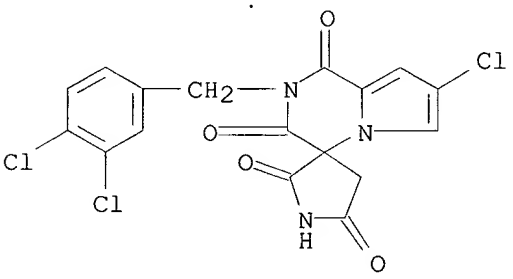


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

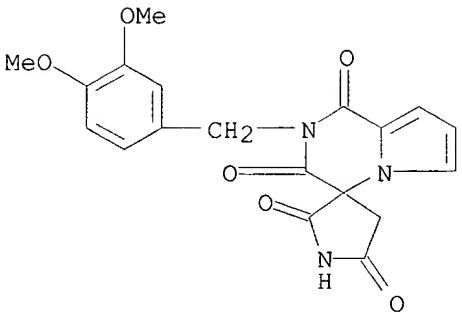
L3 ANSWER 5 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-29-9 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 7'-chloro-2'-[(3,4-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C17 H10 Cl3 N3 O4
SR CA
LC STN Files: CA, CAPLUS



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:83373

L3 ANSWER 6 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-28-8 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(3,4-dimethoxyphenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-71-3
MF C19 H17 N3 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

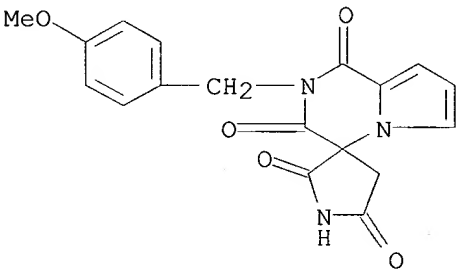


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 7 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-27-7 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-70-2
MF C18 H15 N3 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

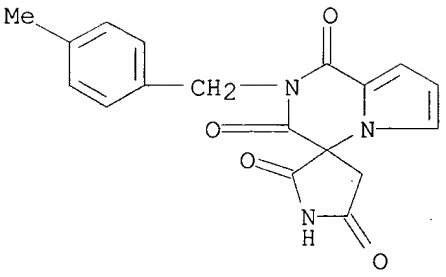


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 8 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-26-6 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-69-9
MF C18 H15 N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

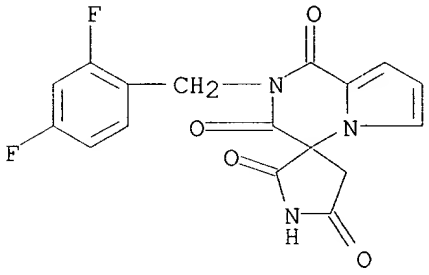


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 9 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-25-5 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(2,4-difluorophenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-68-8
MF C17 H11 F2 N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 10 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-24-4 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)
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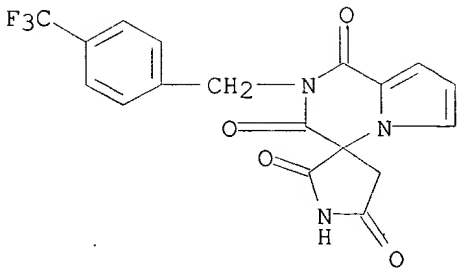
DR 147193-67-7
MF C18 H12 F3 N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

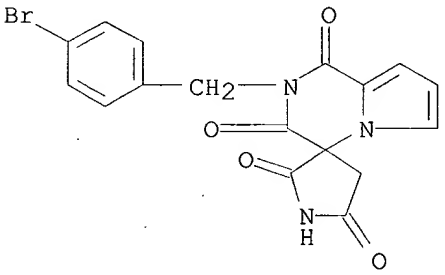


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 11 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-23-3 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromophenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-66-6
MF C17 H12 Br N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

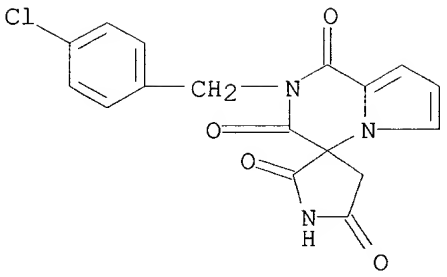


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 12 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-22-2 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-65-5
MF C17 H12 Cl N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 13 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-21-1 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-64-4
MF C17 H12 F N3 O4
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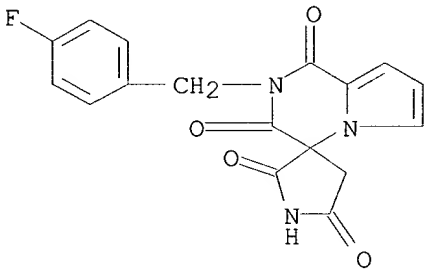
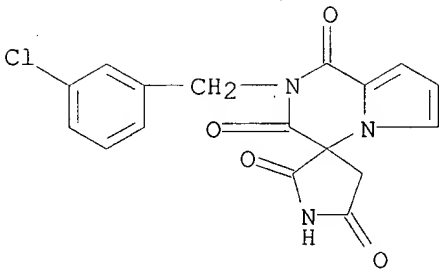


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 14 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-20-0 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(3-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-63-3
MF C17 H12 Cl N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

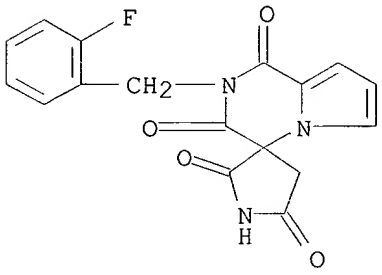


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 15 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-19-7 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-62-2
MF C17 H12 F N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

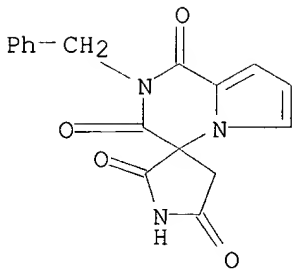


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 16 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-18-6 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-(phenylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-61-1
MF C17 H13 N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

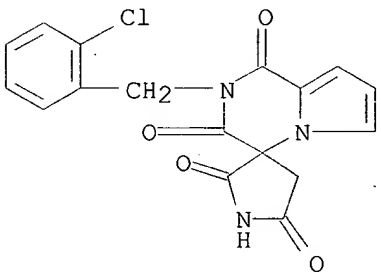


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 17 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-17-5 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(2-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-(2-Chlorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone
FS 3D CONCORD
DR 147193-60-0
MF C17 H12 Cl N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

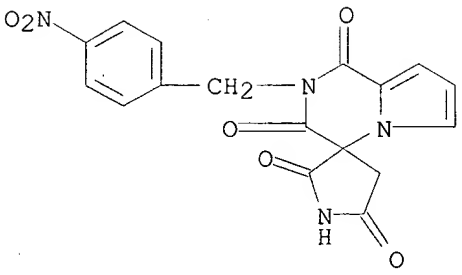


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 18 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156142-16-4 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
DR 147193-73-5
MF C17 H12 N4 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

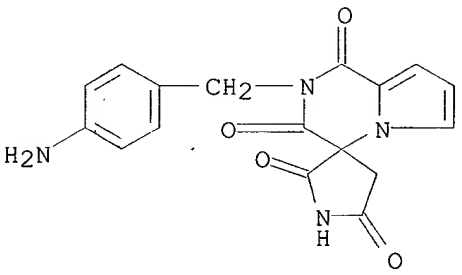


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 19 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156141-94-5 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-aminophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-(4-Aminobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone
FS 3D CONCORD
MF C17 H14 N4 O4
SR CA
LC STN Files: CA, CAPLUS

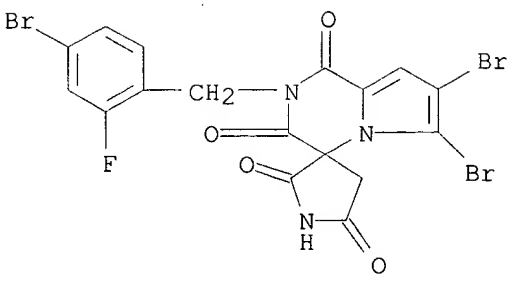


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 20 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156141-93-4 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 6',7'-dibromo-2'-[(4-bromo-2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 6,7-Dibromo-2-(4-bromo-2-fluorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone
FS 3D CONCORD
MF C17 H9 Br3 F N3 O4
SR CA
LC STN Files: CA, CAPLUS

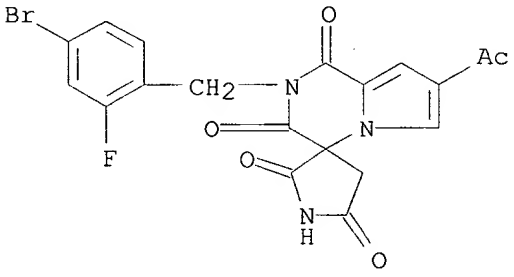


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 121:83373

L3 ANSWER 21 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 156141-85-4 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 7'-acetyl-2'-[(4-bromo-2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 7-Acetyl-2-(4-bromo-2-fluorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone
FS 3D CONCORD
MF C19 H13 Br F N3 O5
SR CA
LC STN Files: CA, CAPLUS

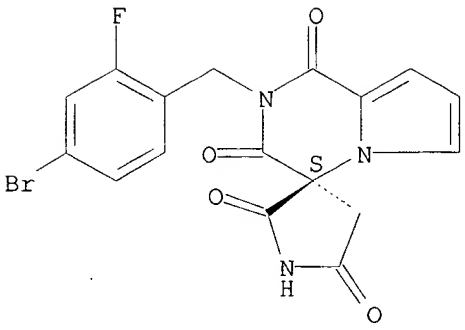


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:83373

L3 ANSWER 22 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147254-65-7 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]-, (3'S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]-, (+)-
FS STEREOSEARCH
MF C17 H11 Br F N3 O4
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, DRUGUPDATES, SYNTHLINE, TOXLIT, USPATFULL

Absolute stereochemistry. Rotation (+).



4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:157023

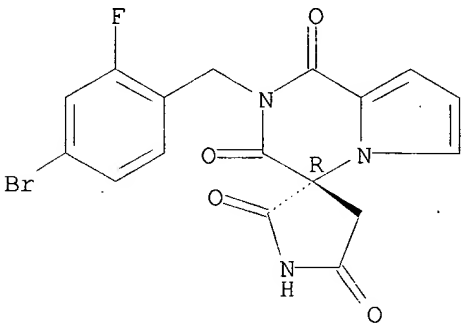
REFERENCE 2: 134:9445

REFERENCE 3: 129:302570

REFERENCE 4: 118:234091

L3 ANSWER 23 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147254-64-6 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]-, (3'R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]-, (-)-
OTHER NAMES:
CN AS 3201
FS STEREOSEARCH
MF C17 H11 Br F N3 O4
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, CIN, DRUGUPDATES, IPA, PHAR, SYNTHLINE, TOXLINE, TOXLIT, USPATFULL

Absolute stereochemistry. Rotation (-).



9 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:157023

REFERENCE 2: 134:9445

REFERENCE 3: 133:171661

REFERENCE 4: 133:144931

REFERENCE 5: 130:316650

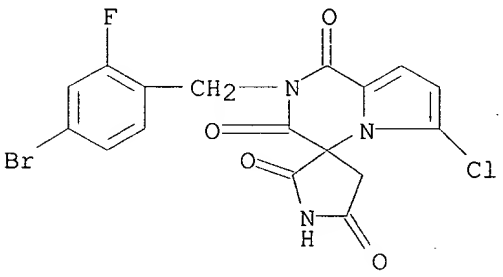
REFERENCE 6: 130:316649

REFERENCE 7: 129:302570

REFERENCE 8: 122:9860

REFERENCE 9: 118:234091

L3 ANSWER 24 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147193-82-6 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]-6'-chloro- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]-6'-chloro-, (.+-.)-
FS 3D CONCORD
MF C17 H10 Br Cl F N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

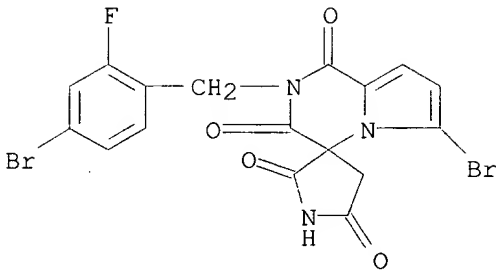


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 118:234091

L3 ANSWER 25 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147193-81-5 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 6'-bromo-2'-[(4-bromo-2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 6'-bromo-2'-[(4-bromo-2-fluorophenyl)methyl]-, (.+-.)-
FS 3D CONCORD
MF C17 H10 Br2 F N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

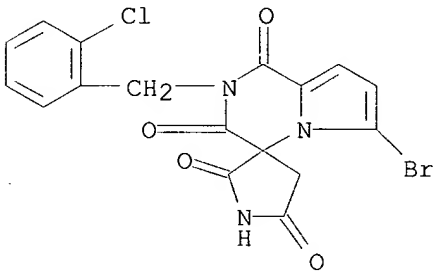


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 118:234091

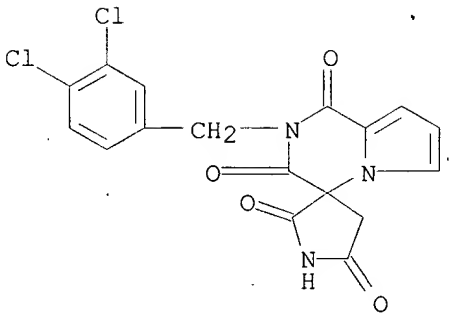
L3 ANSWER 26 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147193-80-4 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 6'-bromo-2'-[(2-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 6'-bromo-2'-[(2-chlorophenyl)methyl]-, (.+-.)-
FS 3D CONCORD
MF C17 H11 Br Cl N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:234091

L3 ANSWER 27 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147193-79-1 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(3,4-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(3,4-dichlorophenyl)methyl]-, (.+-.)-
FS 3D CONCORD
MF C17 H11 Cl2 N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

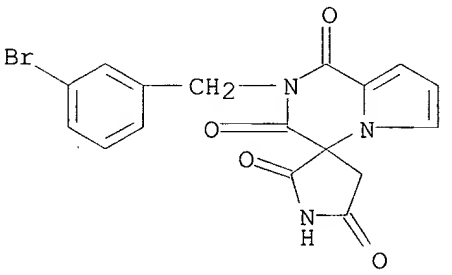


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 118:234091

L3 ANSWER 28 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147193-76-8 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(3-bromophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(3-bromophenyl)methyl]-, (.+-.)-
FS 3D CONCORD
MF C17 H12 Br N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

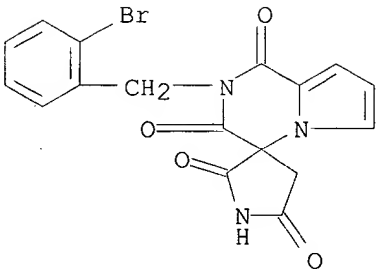


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 118:234091

L3 ANSWER 29 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147193-75-7 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(2-bromophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(2-bromophenyl)methyl]-, (.+-.)-
FS 3D CONCORD
MF C17 H12 Br N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

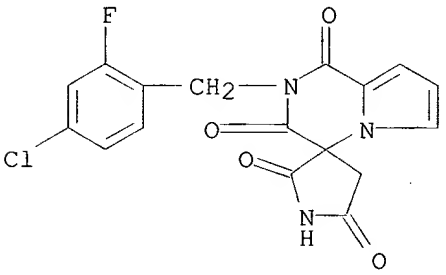


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 118:234091

L3 ANSWER 30 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147193-74-6 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-chloro-2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-chloro-2-fluorophenyl)methyl]-, (.+-.)-
FS 3D CONCORD
MF C17 H11 Cl F N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



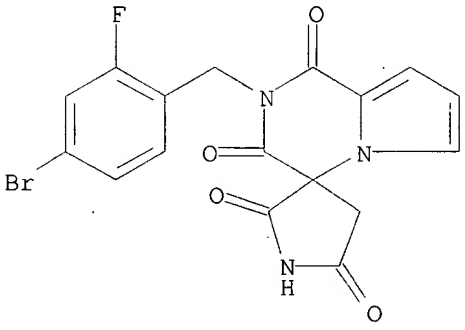
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:302570

REFERENCE 2: 118:234091

L3 ANSWER 31 OF 31 REGISTRY COPYRIGHT 2001 ACS
RN 147193-59-7 REGISTRY
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[pyrrolidine-3,4'(1'H)-pyrrolo[1,2-a]pyrazine]-1',2,3',5(2'H)-tetrone, 2'-[(4-bromo-2-fluorophenyl)methyl]-, (.+-.)-
OTHER NAMES:
CN 2-(4-Bromo-2-fluorobenzyl)-[1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-4-spiro-3'-pyrrolidine]-1,2',3,5'-tetraone
DR 156142-15-3
MF C17 H11 Br F N3 O4
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, DRUGNL, DRUGUPDATES, RTECS*, SYNTHLINE, TOXLIT, USPATFULL

(*File contains numerically searchable property data)



5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:157023

REFERENCE 2: 134:9445

REFERENCE 3: 129:302570

REFERENCE 4: 122:9860

REFERENCE 5: 118:234091